



## SEQUENCE LISTING

<110> BLACK, ROY A.  
PAXTON, RAYMOND JAMES  
BODE, WOLFRAM  
MASCOS, KLAUS  
FERNANDEZ-CATALAN, CARLOS  
CHEN, JAMES MING  
LEVIN, JEREMY IAN

<120> CRYSTALLINE TNF-a-CONVERTING ENZYME AND USES THEREOF

<130> 016761/0170

<140> 09/050,083  
<141> 1998-03-30

<150> 60/073,709  
<151> 1998-02-05

<160> 10

<170> PatentIn Ver. 3.2

<210> 1  
<211> 10  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Illustrative  
peptide

<400> 1  
Pro Leu Ala Gln Ala Val Arg Ser Ser Ser  
1 5 10

<210> 2  
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<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Illustrative  
peptide

<400> 2  
Gly Ser His His His His His His  
1 5

<210> 3  
<211> 11  
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<220>  
 <223> Description of Artificial Sequence: Illustrative  
 peptide

<220>  
 <221> MOD\_RES  
 <222> (3)..(4)  
 <223> variable amino acid

<220>  
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 <223> variable amino acid

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<400> 3  
 His Glu Xaa Xaa His Xaa Xaa Gly Xaa Xaa His  
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<210> 4  
 <211> 203  
 <212> PRT  
 <213> Crotalus adamanteus

<400> 4  
 Glu Gln Asn Leu Pro Gln Arg Tyr Ile Glu Leu Val Val Val Ala Asp  
       1                  5                  10                  15  
 Arg Arg Val Phe Met Lys Tyr Asn Ser Asp Leu Asn Ile Ile Arg Thr  
           20                  25                  30  
 Arg Val His Glu Ile Val Asn Ile Ile Asn Glu Phe Tyr Arg Ser Leu  
           35                  40                  45  
 Asn Ile Arg Val Ser Leu Thr Asp Leu Glu Ile Trp Ser Gly Gln Asp  
       50                  55                  60  
 Phe Ile Thr Ile Gln Ser Ser Ser Asn Thr Leu Asn Ser Phe Gly  
       65                  70                  75                  80  
 Glu Trp Arg Glu Arg Val Leu Leu Thr Arg Lys Arg His Asp Asn Ala  
           85                  90                  95  
 Gln Leu Leu Thr Ala Ile Asn Phe Glu Gly Lys Ile Ile Gly Lys Ala  
           100                  105                  110  
 Tyr Thr Ser Ser Met Cys Asn Pro Arg Ser Ser Val Gly Ile Val Lys  
       115                  120                  125  
 Asp His Ser Pro Ile Asn Leu Leu Val Ala Val Thr Met Ala His Glu  
       130                  135                  140

Leu Gly His Asn Leu Gly Met Glu His Asp Gly Lys Asp Cys Leu Arg  
145 150 155 160

Gly Ala Ser Leu Cys Ile Met Arg Pro Gly Leu Thr Pro Gly Arg Ser  
165 170 175

Tyr Glu Phe Ser Asp Asp Ser Met Gly Tyr Tyr Gln Lys Phe Leu Asn  
180 185 190

Gln Tyr Lys Pro Gln Cys Ile Leu Asn Lys Pro  
195 200

<210> 5

<211> 287

<212> PRT

<213> Homo sapiens

<400> 5

Pro Glu Glu Leu Val His Arg Val Lys Arg Arg Ala Asp Pro Asp Pro  
1 5 10 15

Met Lys Asn Thr Cys Lys Leu Leu Val Val Ala Asp His Arg Phe Tyr  
20 25 30

Arg Tyr Met Gly Arg Gly Glu Glu Ser Thr Thr Thr Asn Tyr Leu Ile  
35 40 45

Glu Leu Ile Asp Arg Val Asp Asp Ile Tyr Arg Asn Thr Ser Trp Asp  
50 55 60

Asn Ala Gly Phe Lys Gly Tyr Gly Ile Gln Ile Glu Gln Ile Arg Ile  
65 70 75 80

Leu Lys Ser Pro Gln Glu Val Lys Pro Gly Glu Lys His Tyr Asn Met  
85 90 95

Ala Lys Ser Tyr Pro Asn Glu Glu Lys Asp Ala Trp Asp Val Lys Met  
100 105 110

Leu Leu Glu Gln Phe Ser Phe Asp Ile Ala Glu Glu Ala Ser Lys Val  
115 120 125

Cys Leu Ala His Leu Phe Thr Tyr Gln Asp Phe Asp Met Gly Thr Leu  
130 135 140

Gly Leu Ala Tyr Val Gly Ser Pro Arg Ala Asn Ser His Gly Gly Val  
145 150 155 160

Cys Pro Lys Ser Gly Ser Ser Gly Gly Ile Cys Glu Lys Ala Tyr Tyr  
165 170 175

Ser Pro Val Gly Lys Lys Asn Ser Lys Leu Tyr Ser Asp Gly Lys Lys  
180 185 190

Lys Glu Ala Asp Leu Val Thr Thr His Glu Leu Gly His Asn Phe Gly  
195 200 205

Ala Glu His Asp Pro Asp Gly Leu Ala Glu Cys Ala Pro Asn Glu Asp  
210 215 220

Gln Gly Gly Lys Tyr Val Met Tyr Pro Ile Ala Val Ser Gly Asp His  
225 230 235 240

Glu Asn Asn Lys Met Phe Ser Asn Cys Ser Lys Gln Ser Ile Tyr Lys  
245 250 255

Thr Ile Glu Ser Lys Ala Gln Glu Cys Phe Gln Glu Arg Ser Asn Lys  
260 265 270

Val Cys Gly Asn Ser Arg Val Asp Glu Gly Glu Glu Cys Asp Pro  
275 280 285

<210> 6

<211> 276

<212> PRT

<213> Homo sapiens

<400> 6

Gln Glu Lys His Ala Ile Asn Gly Pro Glu Leu Leu Arg Lys Arg Arg  
1 5 10 15

Thr Thr Ser Ala Glu Lys Asn Thr Cys Gln Leu Tyr Ile Gln Thr Asp  
20 25 30

His Leu Phe Phe Lys Tyr Tyr Gly Thr Arg Glu Ala Val Ile Ala Gln  
35 40 45

Ile Ser Ser His Val Lys Ala Ile Asp Thr Ile Tyr Gln Thr Thr Asp  
50 55 60

Phe Ser Gly Ile Arg Asn Ile Ser Phe Met Val Lys Arg Ile Arg Ile  
65 70 75 80

Asn Thr Thr Ala Asp Glu Lys Asp Pro Thr Asn Pro Phe Arg Phe Pro  
85 90 95

Asn Ile Ser Val Glu Lys Phe Leu Glu Leu Asn Ser Glu Gln Asn His  
100 105 110

Asp Asp Tyr Cys Leu Ala Tyr Val Phe Thr Asp Arg Asp Phe Asp Asp  
115 120 125

Gly Val Leu Gly Leu Ala Trp Val Gly Ala Pro Ile Tyr Leu Asn Ser  
130 135 140

Gly Leu Thr Ser Thr Ser Leu Asn Thr Gly Ile Ile Thr Val Lys Asn  
145 150 155 160

Tyr Gly Lys Thr Ile Leu Thr Lys Gln Asn Tyr Gly Ser His Val Pro  
165 170 175

Pro Lys Val Ser His Ile Thr Phe Ala His Glu Val Gly His Asn Phe  
180 185 190

Gly Ser Pro His Asp Ser Gly Thr Glu Cys Thr Pro Gly Glu Ser Lys  
 195 200 205  
 Asn Leu Gly Gln Lys Glu Asn Gly Asn Tyr Ile Met Tyr Ala Arg Ala  
 210 215 220  
 Thr Ser Gly Asp Lys Leu Asn Asn Asn Lys Phe Ser Leu Cys Ser Ile  
 225 230 235 240  
 Arg Asn Ile Ser Gln Val Leu Glu Lys Lys Arg Asn Asn Cys Phe Val  
 245 250 255  
 Glu Ser Gly Gln Pro Ile Cys Gly Asn Gly Met Val Glu Gln Gly Glu  
 260 265 270  
 Glu Cys Asp Cys  
 275

<210> 7  
 <211> 824  
 <212> PRT  
 <213> Homo sapiens

<400> 7  
 Met Arg Gln Ser Leu Leu Phe Leu Thr Ser Val Val Pro Phe Val Leu  
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 Ala Pro Arg Pro Pro Asp Asp Pro Gly Phe Gly Pro His Gln Arg Leu  
 20 25 30  
 Glu Lys Leu Asp Ser Leu Leu Ser Asp Tyr Asp Ile Leu Ser Leu Ser  
 35 40 45  
 Asn Ile Gln Gln His Ser Val Arg Lys Arg Asp Leu Gln Thr Ser Thr  
 50 55 60  
 His Val Glu Thr Leu Leu Thr Phe Ser Ala Leu Lys Arg His Phe Lys  
 65 70 75 80  
 Leu Tyr Leu Thr Ser Ser Thr Glu Arg Phe Ser Gln Asn Phe Lys Val  
 85 90 95  
 Val Val Val Asp Gly Lys Asn Glu Ser Glu Tyr Thr Val Lys Trp Gln  
 100 105 110  
 Asp Phe Phe Thr Gly His Val Val Gly Glu Pro Asp Ser Arg Val Leu  
 115 120 125  
 Ala His Ile Arg Asp Asp Asp Val Ile Ile Arg Ile Asn Thr Asp Gly  
 130 135 140  
 Ala Glu Tyr Asn Ile Glu Pro Leu Trp Arg Phe Val Asn Asp Thr Lys  
 145 150 155 160  
 Asp Lys Arg Met Leu Val Tyr Lys Ser Glu Asp Ile Lys Asn Val Ser  
 165 170 175

Arg	Leu	Gln	Ser	Pro	Lys	Val	Cys	Gly	Tyr	Leu	Lys	Val	Asp	Asn	Glu	
			180					185					190			
Glu	Leu	Leu	Pro	Lys	Gly	Leu	Val	Asp	Arg	Glu	Pro	Pro	Glu	Glu	Leu	
		195					200					205				
Val	His	Arg	Val	Lys	Arg	Arg	Ala	Asp	Pro	Asp	Pro	Met	Lys	Asn	Thr	
	210					215					220					
Cys	Lys	Leu	Leu	Val	Val	Ala	Asp	His	Arg	Phe	Tyr	Arg	Tyr	Met	Gly	
225					230					235					240	
Arg	Gly	Glu	Glu	Ser	Thr	Thr	Thr	Asn	Tyr	Leu	Ile	Glu	Leu	Ile	Asp	
				245					250					255		
Arg	Val	Asp	Asp	Ile	Tyr	Arg	Asn	Thr	Ser	Trp	Asp	Asn	Ala	Gly	Phe	
			260					265					270			
Lys	Gly	Tyr	Gly	Ile	Gln	Ile	Glu	Gln	Ile	Arg	Ile	Leu	Lys	Ser	Pro	
		275					280					285				
Gln	Glu	Val	Lys	Pro	Gly	Glu	Lys	His	Tyr	Asn	Met	Ala	Lys	Ser	Tyr	
	290					295					300					
Pro	Asn	Glu	Glu	Lys	Asp	Ala	Trp	Asp	Val	Lys	Met	Leu	Leu	Glu	Gln	
305					310					315					320	
Phe	Ser	Phe	Asp	Ile	Ala	Glu	Glu	Ala	Ser	Lys	Val	Cys	Leu	Ala	His	
				325					330					335		
Leu	Phe	Thr	Tyr	Gln	Asp	Phe	Asp	Met	Gly	Thr	Leu	Gly	Leu	Ala	Tyr	
			340					345					350			
Val	Gly	Ser	Pro	Arg	Ala	Asn	Ser	His	Gly	Gly	Val	Cys	Pro	Lys	Ala	
		355					360					365				
Tyr	Tyr	Ser	Pro	Val	Gly	Lys	Lys	Asn	Ile	Tyr	Leu	Asn	Ser	Gly	Leu	
	370					375					380					
Thr	Ser	Thr	Lys	Asn	Tyr	Gly	Lys	Thr	Ile	Leu	Thr	Lys	Glu	Ala	Asp	
385					390					395					400	
Leu	Val	Thr	Thr	His	Glu	Leu	Gly	His	Asn	Phe	Gly	Ala	Glu	His	Asp	
				405					410					415		
Pro	Asp	Gly	Leu	Ala	Glu	Cys	Ala	Pro	Asn	Glu	Asp	Gln	Gly	Gly	Lys	
			420					425					430			
Tyr	Val	Met	Tyr	Pro	Ile	Ala	Val	Ser	Gly	Asp	His	Glu	Asn	Asn	Lys	
		435					440					445				
Met	Phe	Ser	Asn	Cys	Ser	Lys	Gln	Ser	Ile	Tyr	Lys	Thr	Ile	Glu	Ser	
	450					455					460					
Lys	Ala	Gln	Glu	Cys	Phe	Gln	Glu	Arg	Ser	Asn	Lys	Val	Cys	Gly	Asn	
465					470					475					480	

Ser	Arg	Val	Asp	Glu	Gly	Glu	Glu	Cys	Asp	Pro	Gly	Ile	Met	Tyr	Leu	485	490	495
Asn	Asn	Asp	Thr	Cys	Cys	Asn	Ser	Asp	Cys	Thr	Leu	Lys	Glu	Gly	Val	500	505	510
Gln	Cys	Ser	Asp	Arg	Asn	Ser	Pro	Cys	Cys	Lys	Asn	Cys	Gln	Phe	Glu	515	520	525
Thr	Ala	Gln	Lys	Lys	Cys	Gln	Glu	Ala	Ile	Asn	Ala	Thr	Cys	Lys	Gly	530	535	540
Val	Ser	Tyr	Cys	Thr	Gly	Asn	Ser	Ser	Glu	Cys	Pro	Pro	Pro	Gly	Asn	545	550	555
Ala	Glu	Asp	Asp	Thr	Val	Cys	Leu	Asp	Leu	Gly	Lys	Cys	Lys	Asp	Gly	565	570	575
Lys	Cys	Ile	Pro	Phe	Cys	Glu	Arg	Glu	Gln	Gln	Leu	Glu	Ser	Cys	Ala	580	585	590
Cys	Asn	Glu	Thr	Asp	Asn	Ser	Cys	Lys	Val	Cys	Cys	Arg	Asp	Leu	Ser	595	600	605
Gly	Arg	Cys	Val	Pro	Tyr	Val	Asp	Ala	Glu	Gln	Lys	Asn	Leu	Phe	Leu	610	615	620
Arg	Lys	Gly	Lys	Pro	Cys	Thr	Val	Gly	Phe	Cys	Asp	Met	Asn	Gly	Lys	625	630	635
Cys	Glu	Lys	Arg	Val	Gln	Asp	Val	Ile	Glu	Arg	Phe	Trp	Asp	Phe	Ile	645	650	655
Asp	Gln	Leu	Ser	Ile	Asn	Thr	Phe	Gly	Lys	Phe	Leu	Ala	Asp	Asn	Ile	660	665	670
Val	Gly	Ser	Val	Leu	Val	Phe	Ser	Leu	Ile	Phe	Trp	Ile	Pro	Phe	Ser	675	680	685
Ile	Leu	Val	His	Cys	Val	Asp	Lys	Lys	Leu	Asp	Lys	Gln	Tyr	Glu	Ser	690	695	700
Leu	Ser	Leu	Phe	His	Pro	Ser	Asn	Val	Glu	Met	Leu	Ser	Ser	Met	Asp	705	710	715
Ser	Ala	Ser	Val	Arg	Ile	Ile	Lys	Pro	Phe	Pro	Ala	Pro	Gln	Thr	Pro	725	730	735
Gly	Arg	Leu	Gln	Pro	Ala	Pro	Val	Ile	Pro	Ser	Ala	Pro	Ala	Ala	Pro	740	745	750
Lys	Leu	Asp	His	Gln	Arg	Met	Asp	Thr	Ile	Gln	Glu	Asp	Pro	Ser	Thr	755	760	765
Asp	Ser	His	Met	Asp	Glu	Asp	Gly	Phe	Glu	Lys	Asp	Pro	Phe	Pro	Asn	770	775	780

Ser Ser Thr Ala Ala Lys Ser Phe Glu Asp Leu Thr Asp His Pro Val  
785 790 795 800

Thr Arg Ser Glu Lys Ala Ala Ser Phe Lys Leu Gln Arg Gln Asn Arg  
805 810 815

Val Asp Ser Lys Glu Thr Glu Cys  
820

<210> 8

<211> 477

<212> PRT

<213> Homo sapiens

<400> 8

Met Arg Gln Ser Leu Leu Phe Leu Thr Ser Val Val Pro Phe Val Leu  
1 5 10 15

Ala Pro Arg Pro Pro Asp Asp Pro Gly Phe Gly Pro His Gln Arg Leu  
20 25 30

Glu Lys Leu Asp Ser Leu Leu Ser Asp Tyr Asp Ile Leu Ser Leu Ser  
35 40 45

Asn Ile Gln Gln His Ser Val Arg Lys Arg Asp Leu Gln Thr Ser Thr  
50 55 60

His Val Glu Thr Leu Leu Thr Phe Ser Ala Leu Lys Arg His Phe Lys  
65 70 75 80

Leu Tyr Leu Thr Ser Ser Thr Glu Arg Phe Ser Gln Asn Phe Lys Val  
85 90 95

Val Val Val Asp Gly Lys Asn Glu Ser Glu Tyr Thr Val Lys Trp Gln  
100 105 110

Asp Phe Phe Thr Gly His Val Val Gly Glu Pro Asp Ser Arg Val Leu  
115 120 125

Ala His Ile Arg Asp Asp Asp Val Ile Ile Arg Ile Asn Thr Asp Gly  
130 135 140

Ala Glu Tyr Asn Ile Glu Pro Leu Trp Arg Phe Val Asn Asp Thr Lys  
145 150 155 160

Asp Lys Arg Met Leu Val Tyr Lys Ser Glu Asp Ile Lys Asn Val Ser  
165 170 175

Arg Leu Gln Ser Pro Lys Val Cys Gly Tyr Leu Lys Val Asp Asn Glu  
180 185 190

Glu Leu Leu Pro Lys Gly Leu Val Asp Arg Glu Pro Pro Glu Glu Leu  
195 200 205

Val His Arg Val Lys Arg Arg Ala Asp Pro Asp Pro Met Lys Asn Thr  
210 215 220



Cys	Lys	Leu	Leu	Val	Val	Ala	Asp	His	Arg	Phe	Tyr	Arg	Tyr	Met	Gly	225	230	235	240
Arg	Gly	Glu	Glu	Ser	Thr	Thr	Thr	Asn	Tyr	Leu	Ile	Glu	Leu	Ile	Asp	245	250	255	
Arg	Val	Asp	Asp	Ile	Tyr	Arg	Asn	Thr	Ser	Trp	Asp	Asn	Ala	Gly	Phe	260	265	270	
Lys	Gly	Tyr	Gly	Ile	Gln	Ile	Glu	Gln	Ile	Arg	Ile	Leu	Lys	Ser	Pro	275	280	285	
Gln	Glu	Val	Lys	Pro	Gly	Glu	Lys	His	Tyr	Asn	Met	Ala	Lys	Ser	Tyr	290	295	300	
Pro	Asn	Glu	Glu	Lys	Asp	Ala	Trp	Asp	Val	Lys	Met	Leu	Leu	Glu	Gln	305	310	315	320
Phe	Ser	Phe	Asp	Ile	Ala	Glu	Glu	Ala	Ser	Lys	Val	Cys	Leu	Ala	His	325	330	335	
Leu	Phe	Thr	Tyr	Gln	Asp	Phe	Asp	Met	Gly	Thr	Leu	Gly	Leu	Ala	Tyr	340	345	350	
Val	Gly	Ser	Pro	Arg	Ala	Asn	Ser	His	Gly	Gly	Val	Cys	Pro	Lys	Ala	355	360	365	
Tyr	Tyr	Ser	Pro	Val	Gly	Lys	Lys	Asn	Ile	Tyr	Leu	Asn	Ser	Gly	Leu	370	375	380	
Thr	Ser	Thr	Lys	Asn	Tyr	Gly	Lys	Thr	Ile	Leu	Thr	Lys	Glu	Ala	Asp	385	390	395	400
Leu	Val	Thr	Thr	His	Glu	Leu	Gly	His	Asn	Phe	Gly	Ala	Glu	His	Asp	405	410	415	
Pro	Asp	Gly	Leu	Ala	Glu	Cys	Ala	Pro	Asn	Glu	Asp	Gln	Gly	Gly	Lys	420	425	430	
Tyr	Val	Met	Tyr	Pro	Ile	Ala	Val	Ser	Gly	Asp	His	Glu	Asn	Asn	Lys	435	440	445	
Met	Phe	Ser	Asn	Cys	Ser	Lys	Gln	Ser	Ile	Tyr	Lys	Thr	Ile	Glu	Ser	450	455	460	
Lys	Ala	Gln	Glu	Cys	Phe	Gln	Glu	Arg	Ser	Asn	Lys	Val				465	470	475	

&lt;210&gt; 9

&lt;211&gt; 12

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Description of Artificial Sequence: Illustrative peptide

<400> 9

Ser Pro Leu Ala Gln Ala Val Arg Ser Ser Ser Arg  
1 5 10

<210> 10

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Illustrative  
Met-turn located in SEQ ID NOS 5 & 6

<400> 10

Tyr Val Met Tyr  
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